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REMARKS

Claims 1-46 are pending. Claims 19-46 are withdrawn. Claims 1, 6-8, and 11-18 are amended. Claims 47-58 are new. Support for the amendments can be found in the specification and claims as filed. For example, support for the amendment to claim 1 can be found in claim 6 as originally filed. The new claims do not introduce new matter and are directed to matter disclosed in claims 11-13 and 18 as originally filed.

For the sake of clarity, claim 18 has been amended to delete the superfluous statement "that EC50 is as defined herein." Applicants submit that this amendment is fully supported by the specification and that the definition of EC50 can be found on page 8, lines 8-11 of the PCT application. Additionally, claims 6-8 and 11-18 have been amended to modify their dependencies.

The amendments to the claims should in no way be construed as acquiescence to any of the Examiner's rejections and were made solely to expedite the prosecution of the application. Applicant reserves the right to pursue the claims as originally filed in this or a separate application(s).

Rejections under 35 U.S.C. § 112, second paragraph

The Examiner asserts that claims 1-18 are unclear with regard to the recitation of the phrase "protease assay as described herein." Applicants have amended claim 1 to remove the objected-to phrase, rendering the rejection moot. In addition, claim 1 has been amended to make the solubility factor increase more definite by indicating that it be increased by a factor of more than 1.

The Examiner states that claims 6, 11-13, and 18 are unclear because these claims are directed to both a broad range and a narrow range and that it is unclear whether the narrow range represents a required limitation. Applicants have amended claims 6, 11-13, and 18 so that they are directed solely to the broad range. Applicants have added new claims 47-58 which are directed solely to the narrow ranges. Applicants submit that the claims, as amended, are no longer indefinite

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and respectfully request that the Examiner withdraw the rejection.

Rejections under 35 U.S.C. § 103

The Examiner rejected claims 1-18 under 35 U.S.C. § 103(a) as being unpatentable over Tomalilia et al. (U.S. 5,714,166) in view of Aldrich Technical Publication, 1997 ("Aldrich").

Tomalia et al. describe STARBURST(tm) PAMAM dendrimer conjugates, and go on to describe how the choice of the STARBURST(tm) dendrimer components affects the properties of the dendrimers (col. 12, lines 1-18) further exemplified by Fig 2A and 2B with different branch lengths resulting in distinctly different properties.

Additionally, Tomalia et al. describe dendrimer conjugates comprising biological response modifiers, which are bioactive agents which alter the response of the organism to stimuli, such as but not limited to interleukins, interferons, tumor necrosis factor, granulocyte colony stimulating factor, viruses, viral fragments and other genetic materials (col. 19, lines 33-37). Consequently, the concept of biological response modifiers described in Tomalia et al. does not comprise or suggest dendrimer conjugates for selective solubilisation of protein aggregates according to the claimed invention, as the examiner implicitly seems to contend on page 5 of the office action.

Furthermore, Tomalia et al. describe that the dendrimers can have terminal groups, which are sufficiently reactive to undergo addition or substitution reactions (to make conjugates), and examples of such groups for use with the STARBURST(tm) PAMAM dendrimers include amino, hydroxy, mercapto, carboxy, alkenyl, nitrite, allyl, vinyl, amido, halo, urea, oxiranyl, aziridinyl, oxazolinyl, imidazolinyl, sulfonato, silanyl, phosponato, crown ethers, bipyridines, chloromethylphenyl, isocyanato, and isothiocyanato (col. 30, lines 17-24).

However, Tomalia et al. does not describe or suggest to modify a DAB dendrimer with terminal urea groups for use as a protein solubilising substance, to which the Examiner also fully agrees. But the Examiner looks to the disclosure of Aldrich to find that unmodified DAB(PA)16 diaminobutane dendrimer is commercially available. From this the Examiner asserts that it would have been obvious to one of ordinary skill in the art to provide urea as an end group on

a know PAMAM dendrimer or a known polypropyleneimine dendrimer, such as the DAB-AM-16 disclosed by Aldrich. Applicants respectfully disagree.

It is the burden of the Office to provide a rationale from the prior art for making the specific claimed modification or combination. The Supreme Court recently addressed nonobviousness of "combination" inventions in KSR Co. v. Teletex. Inc., 127 S. Ct. 1727 (2007) (KSR). The Court confirmed that it is legally insufficient to merely point to the various recited elements. Instead, the Office must identify the basis for the alleged modification or combination by one of ordinary skill to arrive at the claimed invention.

> As is clear from cases such as *Adams*, a patent composed of several elements is not proved obvious merely by demonstrating that each of its elements was, independently, known in the prior art. Although common sense directs one to look with care at a patent application that claims as innovation the combination of two known devices according to their established functions, it can be important to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does. This is so because inventions in most, if not all, instances rely upon building blocks long since uncovered, and claimed discoveries almost of necessity will be combinations of what, in some sense, is already known.

Applicants respectfully submit that the Office has failed to meet its burden of providing a rationale for combining the teachings of Tomalia et al. and Aldrich. At the time of the invention neither Tomalia et al. nor Aldrich demonstrated or suggested that there existed a known problem for which the obvious solution would be to modify a DAB dendrimer with a urea terminal group. Indeed, neither Tomalia et al. nor Aldrich provided any other motivation for making the claimed compounds.

Moreover, Tomalia et al. disclose that subtle changes to STARBURST(tm) dendrimers result in distinctly different and unpredictable properties, and that one among many terminal groups which are deemed sufficiently reactive to undergo addition or substitution reactions to make conjugates is urea. The person of skill in the art wanting to solve the problem of providing protein solubilising substances would not be motivated by Tomalia et al. or Tomalia et al. in combination with the Aldrich Catalogue to arrive at a solution falling within the present claims because neither of these references discusses protein solubilisation.

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Furthermore, even if an arbitrary problem could be stated involving the use of urea terminal groups. It is by no means an obvious solution to use the Tomalia et al.'s teaching of STARBURST(tm) dendrimers. One reason being that subtle changes to STARBURST(tm) dendrimers result in distinctly different and <u>unpredictable</u> properties. Given the uncertainty in the combined teachings of Tomalia et al. and Aldrich, a person of skill in the art would not have a reasonable expectation of success of deriving molecules with the claimed properties.

For the reasons discussed, Applicants respectfully request that the foregoing rejections be withdrawn.

<center>CONCLUSION</center>

In view of the above amendment, applicant believes the pending application is in condition for allowance.

Dated: July 28, 2010   Respectfully submitted,

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